REMARKS

The Examiner has indicated that the amendment mailed May 20, 2002, is not fully responsive to the prior Office Action because the marked up version of Claim 24 shows a deletion of "claim" in line 1, and they clean copy of Claim 24 recites in claim in line 1. Also, the marked up copy of claim 23 shows both deletion and insertion of "claim" at the same location in line 1. Applicants appreciate the Examiner's notification of the discrepancies. Applicants respectfully submit that these were inadvertent typographical errors in the Claims. The Claims 23 and 24 provided in each of the Claim sets herein are consistent. The marked up Claims reflect what was filed in the amendment mailed May 20,2002. However, Applicant is unsure of how to indicate that the word "claim" should remain in Claim 23. Thus, Applicant simply indicates that "claim" is part of the Claim. If there are any questions or problems with this format, Applicants would appreciate it if the Examiner would let them know. Applicants wish to confirm that the other amendments presented in the amendment mailed May 20, 2002 have been entered and that Applicants' arguments have been considered. Applicants respectfully submit that in view of the corrections of the typographical errors in Claims 23 and 24 herein, that the Claims are in condition for allowance.

CONCLUSION

In light of the above remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

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APPENDIX I

MARKED-UP VERSION OF REWRITTEN, ADDED, AND/OR CANCELLED CLAIMS

The following is a marked-up version of the Claims, pursuant to 37 C.F.R. §1.121 (c)(1)(ii), with instructions and markings showing changes made herein to the previous version of record of the Specification and Claims. Underlining denotes added text while bracketing denotes deleted text.

Please amend the Claims as follows:

23. (Twice Amended) The method according to claim 20, wherein said epitope of said microbial subtilisin is modified by: (a) substituting the amino acid sequence of the epitope with an analogous sequence from a human homolog of said microbial subtilisin; (b) substituting the amino acid sequence of the epitope with an analogous sequence from a non-human homolog of said microbial subtilisin; or (c) substituting the amino acid sequence of the epitope with a sequence which substantially mimics the major tertiary structure attributes of the epitope.

24. (Twice Amended) The method according to claim 23, wherein the protein is a protease.

APPENDIX II
CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS AS AMENDED IN THIS COMMUNICATION

The following is a list of the Claims as they would appear following entry of this amendment.

17. (Amended) A method for determining a T-cell epitope of a peptide, comprising the steps of:

(a) obtaining from a single human blood source a solution of dendritic cells and a solution of naïve CD4+ and/or CD8+ T-cells;

(b) differentiating said dendritic cells, in said solution of dendritic cells, to produce a solution of differentiated dendritic cells, wherein said differentiating comprises combining said dendritic cells with at least one cytokine;

(c) combining said solution of differentiated dendritic cells and said naïve CD4+ and/or CD8+ T-cells with the peptide, said peptide comprising said T-cell epitope; and

(d) measuring proliferation of said T-cells in said step (c).

18. (Amended) A method of reducing the allergenicity of a protein comprising the steps of:

(a) identifying a T-cell epitope in said protein by

(i) contacting an adherent monocyte-derived dendritic cell that has been differentiated by exposure to at least one cytokine *in vitro*, with a peptide comprising said T-cell epitope; and

(ii) contacting said dendritic cell and peptide with a naïve T-cell, wherein said naïve T-cell has been obtained from the same source as said adherent monocyte-derived dendritic cell, and whereby said T-cell proliferates in response to said peptide; and

(b) modifying said protein to neutralize said T-cell epitope such that the modified protein induces less than or substantially equal the baseline proliferation of said naïve T-cells.

19. The method according to claim 18, wherein the protein is a protease.

20. (Amended) A method for reducing the allergenicity of a microbial subtilisin comprising the steps of:

(a) determining a T-cell epitope of said subtilisin comprising (i) obtaining from a from a single human blood source a solution of dendritic cells and a solution of naïve CD4+ and/or CD8+ T-cells; (ii) promoting differentiation in said solution of dendritic cells; combining said solution of differentiated dendritic cells and said naïve CD4+ and/or CD8+ T-cells with peptide fragments of said subtilisin; and (iv) measuring proliferation of said T-cells in said step (iii); and

(b) modifying the peptide which includes the T-cell epitope to neutralize said epitope.

21. The method according to claim 20, wherein the microbial subtilisin is derived from a *Bacillus*.

22. The method according to claim 21, wherein the *Bacillus* is selected from the group consisting of *B. lentus, B. subtilisin, B. amyloliquefaciens* and *B. licheniformis*.

23. (Amended) The method according to claim 20, wherein said epitope of said microbial subtilisin is modified by: (a) substituting the amino acid sequence of the epitope with an analogous sequence from a human homolog of said microbial subtilisin; (b) substituting the amino acid sequence of the epitope with an analogous sequence from a non-human homolog of said microbial subtilisin; or (c) substituting the amino acid sequence of the epitope with a sequence which substantially mimics the major tertiary structure attributes of the epitope.

24. (Amended) The method according to claim 23, wherein the protein is a protease.

25. The method according to claim 24, wherein the protease is a subtilisin.

29. The method according to claim 18, wherein said T-cell epitope is modified by a substitution selected from the group consisting of:

(a) substituting the amino acid sequence of said T-cell epitope with an analogous sequence from a human homolog to the protein of interest;

(b) substituting the amino acid sequence of said T-cell epitope with an analogous sequence from a non-human homolog to the protein of interest; or

(c) substituting the amino acid sequence of said T-cell epitope with a sequence which substantially mimics the major tertiary structure attributes of the epitope.

30. The method according to claim 29, wherein said T-cell epitope is modified by substituting the amino acid sequence of the T-cell epitope with an analogous sequence from a human homolog to the protein of interest.

31. The method according to claim 29, wherein said T-cell epitope is modified by substituting the amino acid sequence of said T-cell epitope with an analogous sequence from a non-human homolog to the protein of interest.

32. The method according to claim 29, wherein said T-cell epitope is modified by substituting the amino acid sequence of the epitope with a sequence which substantially mimics the major tertiary structure attributes of said T-cell epitope.